AGE SPECIFIC CHANGES IN LEFT VENTRICULAR RELAXATION: A DOPPLER ECHOCARDIOGRAPHY STUDY IN HEALTHY EGYPTIAN INDIVIDUALS

Thesis

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التغيرات المرتبطة بالعمر والنوع فى استرخاء البطين الأيسر: دراسة الفحص الصدوى بالدوبلر على القلب لدى الأشخاص الأصحاء

رسالة

توطئة للحصول علي درجة الماجيستير
في أمراض القلب

مقدمة من

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SUMMARY

Cardiovascular disease affects men and women differently. women are more likely to have heart failure with a preserved ejection fraction (HFpEF) [٢٦١]. Population-based studies consistently demonstrate a female predominance in HFpEF, particularly among the elderly, yet the causes for this unequal distribution of the sexes in HFpEF remain unclear. [٢٦٧]

In the present study we examined ٢١٩ healthy male and ١٨٨ healthy female, aged ١٨y–٦٠ years, with standard echocardiography and tissue Doppler imaging.

We divided the subjects into ٤ groups based on their age: (١٨y- ٢٩y), (٣٠y – ٣٩y), (٤٠y -٤٩y), and ((٥٠y -٥٩y). For each patient a full history was taken with general examination and ECG was done then transthoracic Echocardiography, the following measurements were taken, systolic function assessed by; LV internal dimensions, Ejection fraction, Fractional shortening.

Diastolic function assessed by: Mitral inflow early diastolic velocity (E), late diastolic velocity (A) and E/A assessed by applying pulsed wave Doppler**,** Deceleration time of early mitral inflow**,** with the use of tissue Doppler imaging early (E`) and late (A`) diastolic annular velocities as well as systolic annular velocity (S`) were measured. Also E/Ea was calculated.

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List of Abbreviations

LV.....	: left ventricle.
EF	: Ejection fraction
HFNEF.....	: Heart failure with normal ejection fraction
ECG	: Electrocardiogram
TDI	: Tissue Doppler imaging
LVSF	: Lt. Ventricular systolic function
PCWP	: Pulmonary capillary wedge pressure
LVEDP	: Lt. ventricular end diastolic pressure
LVP.....	: Lt. ventricular pressure
SR	: Sarcoplasmic reticulum
SERCA	: $Ca^{٢}$ +adenosine triphosphate of the sarcoplasmic reticulum
DHF	: Diastolic heart failure
MMPs	: Matrix metalloproteinases
LA.....	: Lt. Atrium
DT.....	: Deceleration time
AV	: Atrioventricular valves
PA.....	: Pulmonary artery
TR.....	: Tricuspid regurgitation
CW.....	: Continuous wave
PR	: Pulmonary regurgitation
PNF.....	: Pseudo normal Lt. ventricular filling
IVRT.....	: Isovolumic relaxation time
MR.....	: mitral regurgitation.
Vp	: Flow propagation velocity
CHF	: Congestive heart failure
PKA	: Protein kinase A
HRT	: Hormone replacement therapy
VSMCs	: Vascular smooth muscle cells
ERB	: Estrogen receptor B
NO	: Nitric oxide
Ed.....	: Diastolic elastance
Ees	: End-systolic elastance
EDD.....	: End diastolic diameter
ESD.....	: End systolic diameter
BMI.....	: Body mass index
FS.....	: Fractional shortening

INTRODUCTION

Over the past ٢٠ years, the number of cardiovascular deaths for women has exceeded those for men.[١] Gender-specific differences in the cause or prognosis of heart failure, may in part explain this excess mortality in women.[٢] Pathophysiological and clinical presentation of women with heart failure may be different from those of men. In women, heart failure tends to be associated with impaired diastolic function or diastolic heart failure rather than systolic heart failure, which is a predominant cause of heart failure in men.[٣–٦]

The normal aging process is associated with changes in myocardial structure and function.[٧,٨] It is well known that left ventricular (LV) systolic function at rest appears to be unaffected by aging.[٩-١١] In contrast, many studies in human subjects have shown that LV diastolic function, as estimated by analysis of early diastolic filling velocity-deteriorates with aging.[١٢-١٥] The mechanisms underlying this change in diastolic function are not fully understood, but the change may result in part from age-related decrease in the rate of LV relaxation. Previous experimental studies[١٦-١٨] demonstrated that the duration of isometric contraction and the time to peak tension were prolonged in senescent rats.

Normal healthy aging results in changes in Doppler indexes of diastolic function, including a prolongation of the isovolumetric relaxation time (IVRT), a reduction in the E-wave velocity of early

mitral inflow compared with the late atrial wave (A), and a slower deceleration time of early mitral filling.[١٩-٢١] these parameters depend in part, on the relationship between left atrial pressure (LAP) and the ventricular properties of relaxation and compliance.[٢٢]

Biologic changes associated with age may be an important factor underlying the association between increasing age and the prevalence of preserved LVSF in HF. Normal aging is associated with interstitial fibrosis[٢٣] and myocardial hypertrophy[٢٤], which can result in abnormal LV relaxation and compliance. Aging has also been associated with changes in intra-cardiac blood flow patterns, reflecting alterations in diastolic function [٢٥].

Biologic factors may also underlie the observed relationship between female gender and preserved LVSF. Prior research has identified differences between men and women in changes in LV geometry and wall thickness as a response to chronic pressure overload. Among patients with severe aortic stenosis, Carroll et al. found differences in LV adaptation to chronic pressure overload between men and women. Among patients with similar degrees of LV outflow obstruction and symptoms, women had higher indices of LV function and lower degrees of wall stress than men [٢٦].

Among this older population hospitalized with HF, the correlation between female gender and preserved LVSF was seen in patients with or without hypertension, arrhythmia, valvular disease, or renal insufficiency. Even among patients with prior

myocardial infarction, women were more likely to have preserved LVSF, which raises the possibility of gender differences in ventricular remodeling post-infarction. The consistency of the association between gender and preserved LVSF across numerous subgroups of patients implies that gender itself is likely an important determinant of LV adaptation regardless of the underlying pathologic processes associated with the development of HF.

Previously, better survival among women had been attributed to better systolic function, and women were thought to have more hospitalization over time but now.

Even with systolic dysfunction, women have better survival compared with men and that hospitalization over time is influenced more by etiology than gender[٢٩-٣٤].

Tissue Doppler imaging (TDI) technology has become one of the standard methods to assess (LV) diastolic function and provide pathophysiological as well as prognostic insight into systolic and diastolic heart failure.[٧-١١]

Because of its high reproducibility, feasibility, and relatively preload independence, tissue Doppler recording of the early diastolic mitral annular velocity (E') in conjunction with the mitral inflow velocity (E) has become the first line of diastolic evaluation. Myocardial relaxation is impaired in almost all patients with diastolic dysfunction, which is best assessed by the E' velocity of

the mitral annulus using TDI and which remains decreased at all stages of diastolic dysfunction (٣٥), However, early diastolic trans-mitral velocity (E) increases progressively as LV filling pressure increases with worsening of the grade of diastolic dysfunction.

AIM OF THE WORK

The aim of this study is to investigate age- and gender-specific changes in tissue Doppler–derived left ventricular diastolic index (E').